nucleotides 568 to 2045 of SEQ ID NO: 1; (c) a nucleic acid sequence which hybridizes under medium stringency conditions with (i) nucleotides 568 to 2045 of SEQ ID NO: 1, (ii) the cDNA sequence contained in nucleotides 568 to 2045 of SEQ ID NO: 1, or (iii) a complementary strand of (i) or (ii); and (d) a subsequence of (a), (b), or (c), wherein the subsequence encodes a polypeptide fragment which has phospholipase B activity.

Applicant has shown that the closest protein with any identity to the instant phospholipase B is a phospholipase C, not a phospholipase B. A comparative alignment performed by Applicant showed that the *Aspergillus oryzae* HowB430 phospholipase B shares 26% identity with a phospholipase C from *Pseudomonas aeruginosa* (SwissProt Acc. No. P15713) (see Example 4 of the specification). Applicant has, therefore, discovered a new class of phospholipase B, with only a very distant relationship to known phospholipases C, but no relationship to known phospholipases B. The Office Action supports Applicant's position by stating: "A search of the protein databases by the PTO failed to reveal that any prior art phospholipase B ... shares significant homology with the instant phospholipase B." However, the Office Action asserts that the claims should be limited to the nucleic acid sequence of SEQ ID NO: 1 or the amino acid sequence of SEQ ID NO: 2.

Claims limited to the nucleic acid sequence of SEQ ID NO: 1 or the amino acid sequence of SEQ ID NO: 2 would not adequately protect the invention from copyists who could otherwise make a minor change to the sequence and thereby avoid infringement while still exploiting the benefits of Applicant's invention. For example, one of ordinary skill in the art could circumvent Applicant's patent rights by making one or more conservative amino acid changes in the sequence of SEQ ID NO: 2. Such conservative substitutions can be, for example, within the group of basic amino acids (arginine, lysine and histidine), acidic amino acids (glutamic acid and aspartic acid), polar amino acids (glutamine and asparagine), hydrophobic amino acids (leucine, isoleucine and valine), aromatic amino acids (phenylalanine, tryptophan and tyrosine), and small amino acids (glycine, alanine, serine, threonine and methionine). Thus, based on the teachings of the present application, one skilled in the art could exploit the benefits of Applicant's invention by constructing or finding another phospholipase B having essentially the same properties of the phospholipase B of the instant invention and thereby circumvent the literal scope of Applicant's patent rights should the claims be limited to the nucleic acid sequence of SEQ ID NO: 1 or the amino acid sequence of SEQ ID NO: 2.

The *Regents of the University of California v. Eli Lilly & Co.* Court stated that an adequate written description of genetic material requires a precise definition, such as by structure, formula, chemical name, or physical properties. *Regents of the University of California v. Eli Lilly & Co.,* 119 F.3d 1559, 1566 43 USPQ2d 1398, 1404 (Fed.Cir.1997) (quoting *Fiers,* 984 F.2d at 1171, 25 USPQ2d

at 1606). Applicant submits that the properties of hybridization under stringency conditions and percent identity satisfy the requirement enunciated in *Regents of the University of California v. Eli Lilly & Co.* decision.

Applicant asserts that the written description requirement is met for all of the claimed nucleic acid sequences on the basis of the functional ability of the claimed nucleotide sequences to hybridize to the nucleic acid sequence of SEQ ID NO: 1, which is accessible from the Agricultural Research Service Patent Culture Collection, Peoria, Illinois, under accession number NRRL B-30142. The claimed nucleic acid sequences are adequately described on the basis of the function of hybridization by their affinity under stringency conditions to the mature coding region of SEQ ID NO: 1 because the function of hybridization inherently specifies structure. If the claimed nucleic acid sequences hybridize under the disclosed stringency conditions to the mature coding region of SEQ ID NO: 1, such hybridization properties dictate that all species within the genus will be structurally similar.

Applicant also asserts that the written description requirement is met for all of the claims on the basis of percent identity. The claimed nucleic acid sequences are adequately described on the basis of comparing percent identity of an encoded phospholipase B to the mature polypeptide of SEQ ID NO: 2 because percent identity of a polypeptide having phospholipase B activity inherently specifies structure. If the amino acid sequence encoded by a claimed nucleic acid sequence has at least 80% identity with amino acids 20 to 464 of SEQ ID NO: 2, such percent identity properties dictate that all species within the genus will be structurally similar.

The Office Action of December 7, 2001, stated that "[a]ll the specification does is provide a possible plan for obtaining other nucleic acid sequences embraced by the claims, the success of which is completely unclear." Applicant respectfully disagrees. A person of skill in the art, with the accession number NRRL B-30142 provided in the specification, can obtain the claimed sequence of SEQ ID NO: 1 from the Agricultural Research Service Patent Culture Collection and follow the appropriate techniques described in Applicant's specification to excise the nucleotide sequence from the deposited organism. Applicant has detailed on page 5, line 1, to page 7, line 7, of the specification, instructions for performing standard Southern hybridization under medium, medium-high, and high stringency conditions to identify such nucleic acids from other strains, whether of the same or different genera or species. Applicant also details on page 3, line 25, to page 4, line 7, of the specification, instructions for determining the degree of identity between two amino acid sequences by the Clustal method (Thompson *et al.*, 1994, *Nucleic Acids Research* 22: 4673-4680; Thompson *et al.*, 1997, *Nucleic Acids Research* 25: 4876-4882), and on page 12, line 29, to page 13, line 8, of the specification, the degree of homology between two nucleic acid sequences by the Wilbur-Lipman method (Wilbur and Lipman,

1983, *Proceedings of the National Academy of Science USA* 80: 726-730). These methods are highly predictable and do not require undue experimentation.

The written description as a whole is sufficient to evidence possession of the claimed nucleic acid sequences because the sequences are defined by relation to the structure of the sequence of SEQ ID NO: 1 as well as the inherent properties of the polypeptide encoded by the nucleic acid sequences of SEQ ID NO: 1. Thus, there is sufficient written description in the specification to show that the inventors, at the time the application was filed, had possession of the claimed invention.

For the foregoing reasons, Applicant submits that the rejections under 35 U.S.C. § 112 have been overcome. Applicant respectfully requests reconsideration and withdrawal of the rejections.

II. The Rejection of Claims 100-104, 108-111, 113-115, and 117-124 under 35 U.S.C. § 112, First Paragraph

Claims 100-104, 108-111, 113-115, and 117-124 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid sequence encoding phospholipase B wherein either the nucleic acid sequence comprises nucleotides 568 to 2045 of SEQ ID NO: 1 or the polypeptide comprises amino acids 20-464 of SEQ ID NO: 2, does not reasonably provide enablement for any other embodiments lying outside this scope. This rejection is respectfully traversed.

A person of skill in the art, with the accession number NRRL B-30142 provided in the specification, can obtain the claimed sequence of SEQ ID NO: 1 from the Agricultural Research Service Patent Culture Collection and follow the appropriate techniques described in Applicant's specification to excise the nucleotide sequence from the deposited organism. Applicant submitted a Statement under 37 C.F.R. § 1.808 that *E. coli* NRRL B-30142 was deposited under the Budapest Treaty and all restrictions will be removed upon the granting of the U.S. patent. Applicant has also provided detailed instructions on page 5, line 1, to page 7, line 7, of the specification, for performing standard Southern hybridization under medium and high stringency conditions to identify genes encoding the polypeptides of the instant invention from other strains of different genera or species. Applicant discloses the following probes in the specification for use in conducting the hybridization: (i) nucleotides 568 to 2045 of SEQ ID NO: 1, (ii) the cDNA sequence contained in nucleotides 568 to 2045 of SEQ ID NO: 1, and (iii) a complementary strand of (i) or (ii). These probes consist of the mature coding region of SEQ ID NO: 1, which is the most essential part of the entire phospholipase B gene. The use of these nucleotide sequences as probes enables the identification and isolation of other genes that are closely related or essentially identical to the gene of SEQ ID NO: 1 encoding a

polypeptide having phospholipase B activity. For example, Applicant has provided details in Example 2 for probing a DNA library of an *Aspergillus* strain. Once a gene is isolated and its nucleotide sequence determined, the nucleotide sequence and the deduced amino acid sequence thereof can then be compared to SEQ ID NO: 1 and SEQ ID NO: 2, respectively, to ascertain whether the gene falls within the scope of the instant claims. Applicant has provided detailed instructions on page 3, line 25, to page 4, line 7, of the specification, for determining the degree of identity between two amino acid sequences by the Clustal method (Thompson *et al.*, 1994, *Nucleic Acids Research* 22: 4673-4680; Thompson *et al.*, 1997, *Nucleic Acids Research* 25: 4876-4882), and on page 12, line 29, to page 13, line 8, of the specification, the degree of homology between two nucleic acid sequences by the Wilbur-Lipman method (Wilbur and Lipman, 1983, *Proceedings of the National Academy of Science USA* 80: 726-730). Moreover, using Applicant's specification, production of the phospholipase B can be achieved and enzymatically assayed to show it has phospholipase B activity.

Applicant submits, therefore, that the information disclosed in the specification combined with the knowledge of the art provides sufficient guidance to one of ordinary skill in the art to isolate such nucleic acids from other strains. Thus, there is sufficient enabling description in the specification to direct and guide the skilled artisan to practice the claimed invention.

For the foregoing reasons, Applicant submits that the rejections under 35 U.S.C. § 112 have been overcome. Applicant respectfully requests reconsideration and withdrawal of the rejections.

III. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

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